

Appl. No. 09/393,590
Amendment dated March 9, 2005
Reply to Office Action of June 1, 2004

Amendments to the Claims:

1. (Currently Amended) A stable liquid pharmaceutical botulinum toxin formulation, comprising
a pharmaceutically acceptable buffer buffered saline capable of providing a buffered pH range between ~~about~~ pH 5 and pH 6 + 10%, and
purified botulinum toxin;
wherein said formulation is stable as a liquid for at least one year at a temperature between ~~about~~ 0 and 10 degrees centigrade + 10%.
2. (Currently Amended) The formulation of claim 1, wherein said temperature is ~~about~~ 5+3 degrees centigrade.
3. (Currently Amended) The formulation of claim 1, wherein said temperature is ~~about~~ 4+2 degrees centigrade.
4. (Currently Amended) The formulation of claim 1, wherein said buffered pH range is ~~about~~ pH 5.6+[[0.2]] 10%.
5. (Original) The formulation of claim 1, wherein said toxin formulation is stable in liquid form for at least two years.
6. (Original) The formulation of claim 1, wherein said buffer has a pK in the range of pH 4.5-6.5.
7. (Original) The formulation of claim 6, wherein said buffer is selected from the group consisting of phosphate buffer, phosphate-citrate buffer, and succinate buffer.

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8. (Previously Presented) The formulation of claim 1, wherein said botulinum toxin is of a botulinum toxin type selected from the group consisting of Types A, B, C₁, C₂, D, E, F and G.
9. (Currently Amended) The formulation of claim 8, wherein said botulinum toxin is botulinum toxin Type B present at a concentration in the range of ~~about~~ 100-20,000 U/ml + 10%.
10. (Currently Amended) The formulation of claim 9, wherein said botulinum toxin Type B is present in a high molecular weight complex of ~~about~~ 700 kilodaltons (kD) + 10%.
11. (Currently Amended) The formulation of claim 9, wherein said botulinum toxin Type B is present at a concentration between ~~about~~ 1000-5000 U/ml.
12. (Currently Amended) The formulation of claim 8, wherein said botulinum toxin is botulinum toxin Type A, present at a concentration in the range of ~~about~~ between 20-2000 U/ml.
13. (Currently Amended) The formulation of claim 12, wherein said botulinum toxin Type A is present at a concentration in the range of ~~about~~ between 100-1000 U/ml.
14. (Original) The formulation of claim 1, which further includes an excipient protein.
15. (Original) The formulation of claim 14, wherein said excipient protein is selected from the group consisting of serum albumin, recombinant human serum albumin, and gelatin.
16. (Currently Amended) A stable liquid pharmaceutical botulinum toxin formulation, comprising
a pharmaceutically acceptable liquid ~~buffer~~ buffered saline capable of providing a buffered pH range between ~~about~~ pH 5 and pH 6 + 10%, and
purified botulinum toxin;
wherein said toxin formulation is stable as a liquid for at least about 6 months at a temperature between ~~about~~ 10 and 30 degrees centigrade + 10%.

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17. (Currently Amended) The formulation of claim 16, wherein said temperature is ~~about~~ 25°C + 10%.

18. (Currently Amended) The formulation of claim 16, wherein said buffered pH range is ~~about~~ pH 5.6, ~~+ [[0.2]]~~ + 10%.

19. (Currently Amended) The formulation of claim 16, wherein said buffer has a pK in the range of pH between 4.5-6.5.

20. (Original) The formulation of claim 19, wherein said buffer is selected from the group consisting of phosphate buffer, phosphate-citrate buffer, and succinate buffer.

21. (Previously Presented) The formulation of claim 16, wherein said botulinum toxin is of a botulinum toxin type selected from the group consisting of Types A, B, C₁, C₂, D, E, F and G.

22. (Currently Amended) The formulation of claim 21, wherein said botulinum toxin is botulinum toxin Type B present at a concentration of ~~about~~ between 100-20,000 U/ml + 10%.

23. (Currently Amended) The formulation of claim 22, wherein said botulinum toxin Type B is present in a high molecular weight complex of ~~about~~ 700 kD + 10%.

24. (Currently Amended) The formulation of claim 22, wherein said botulinum toxin Type B is present at a concentration in the range of ~~about~~ between 1000-5000 U/ml.

25. (Currently Amended) The formulation of claim 21, wherein said botulinum toxin is botulinum toxin Type A, present at a concentration in the range of ~~about~~ between 20-2000 U/ml.

26. (Currently Amended) The formulation of claim 25, wherein said botulinum toxin is botulinum toxin Type A, present at a concentration in the range of ~~about~~ between 100-1000 U/ml.

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27. (Original) The formulation of claim 16, which further includes an excipient protein.

28. (Original) The formulation of claim 25, wherein said excipient protein is selected from the group consisting of serum albumin, human serum albumin, and gelatin.

29. (Withdrawn) A method of treating a patient in need of inhibition of cholinergic input to a selected muscle, muscle group, gland or organ, comprising administering to the selected muscle, muscle group, gland or organ of the patient a pharmaceutically effective dose of liquid botulinum toxin formulation which includes a pharmaceutically acceptable buffer capable of providing a buffered pH range between about pH 5 and pH 6, and

isolated botulinum toxin;

wherein said toxin formulation is stable as a liquid for at least one year at a temperature between about 0 and 10 degrees centigrade or for at least six months at a temperature between about 10 and 30 degrees centigrade.

30. (Withdrawn) The method of claim 29, wherein said patient is suffering from a disorder selected from the group consisting of spasticity, blepharospasm, strabismus, hemifacial spasm, dystonia, otitis media, spastic colitis, animus, urinary detrusor-sphincter dyssynergia, jaw-clenching, and curvature of the spine.

31. (Withdrawn) The method of claim 30, wherein said patient is suffering from spasticity due to one or more of the group consisting of stroke, spinal cord injury, closed head trauma, cerebral palsy, multiple sclerosis, and Parkinson's disease.

32. (Withdrawn) The method of claim 30, wherein said patient is suffering from a dystonia selected from the group consisting of spasmodic torticollis (cervical dystonia), spasmodic dysphonia, limb dystonia, laryngeal dystonia, and oromandibular (Meige's) dystonia.

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33. (Withdrawn) The method of claim 29, wherein said selected muscle or muscle group produces a wrinkle or a furrowed brow.
34. (Withdrawn) The method of claim 29, wherein said muscle is a perineal muscle and wherein said patient is in the process of giving birth to a child.
35. (Withdrawn) The method of claim 29, wherein said patient is suffering from a condition selected from the group consisting of myofascial pain, headache associated with migraine, vascular disturbances, neuralgia, neuropathy, arthritis pain, back pain, hyperhydrosis, rhinorrhea, asthma, excessive salivation, and excessive stomach acid secretion.
36. (Withdrawn) The method of claim 29, wherein said formulation is stable as a liquid for at least one year at a temperature of about 5 ± 3 degrees centigrade.
37. (Withdrawn) The method of claim 29, wherein said formulation is stable as a liquid for at least one year at a temperature of about 4 ± 2 degrees centigrade.
38. (Withdrawn) The method of claim 29, wherein said formulation is stable as a liquid for at least two years at a temperature between about 0 and 20 degrees centigrade.
39. (Withdrawn) The method of a claim 29, wherein said buffered pH range is about pH 5.6 ± 0.2
40. (Withdrawn) The method of claim 29, wherein said buffer has a pK in the range of pH 4.5-6.5.
41. (Withdrawn) The method of claim 29, wherein said buffer is selected from the group consisting of phosphate buffer, phosphate-citrate buffer, and succinate buffer.

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42. (Withdrawn) The method of claim 29, wherein said botulinum toxin is a botulinum toxin serotype selected from the group consisting of serotypes A, B, C₁, C₂, D, E, F and G.
43. (Withdrawn) The method of claim 42, wherein said botulinum toxin is botulinum toxin Type B present at a concentration in the range of about 100-20,000 U/ml.
44. (Withdrawn) The method of claim 43, wherein said botulinum toxin Type B is present in a high molecular weight complex of about 700 kD.
45. (Withdrawn) The method of claim 43, wherein said botulinum toxin Type B is present at a concentration of about 1000-5000 U/ml.
46. (Withdrawn) The method of claim 42, wherein said botulinum toxin is botulinum toxin Type A, present at a concentration in the range of about 20-2000 U/ml.
47. (Withdrawn) The method of claim 46, wherein said botulinum toxin Type A is present at a concentration in the range of about 100-1000 U/ml.
48. (Withdrawn) The method of claim 29, which further includes an excipient protein.
49. (Withdrawn) The method of claim 48, wherein said excipient protein is selected from the group consisting of serum albumin, recombinant human serum albumin, and gelatin.
50. (Withdrawn) The method of claim 29, wherein said patient is refractory to botulinum toxin Type A and said botulinum toxin in said formulation is selected from the group consisting of botulinum serotypes B, C₁, C₂, D, E, F and G.
51. (Withdrawn) The method of claim 50, wherein said botulinum toxin in said formulation is botulinum toxin Type B.

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52. (Withdrawn) The method of claim 29, wherein said patient is refractory to botulinum toxin Type B and said botulinum toxin in said formulation is selected from the group consisting of botulinum serotypes A, C₁, C₂, D, E, F and G.

53. (Withdrawn) The method of claim 52, wherein said botulinum toxin in said formulation is botulinum toxin Type A.